Center Reflections

A monthly publication highlighting activities at the W.M. Keck Foundation Center for Molecular Structure

California State University Fullerton

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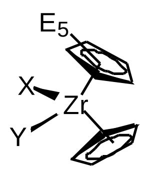
Lewis Acidic Zirconium Complexes Based on Cationic Sandwich and Neutral Piano Stool Structures

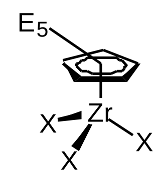
CSU Los Angeles

The research being undertaken by Prof. Wayne Tikkanen at CSU Los Angeles is the preparation and testing of zirconium based Lewis acids to promote stereoselective organic transformations. The applications of Lewis acids are broad and span a wide range of reactions. Lewis acid catalysts promote many reactions more readily and specifically (regio- and stereo-selectivity). Readily resolvable transition metal Lewis acid catalysts based on metallocenes of C_2 symmetry or lower have been successful in promoting a variety of reactions.

Tikkanen and his students are synthesizing asymmetric transition metal based Lewis acids based on the compound types **B** and **C** shown above right, where E = methyl or phenyl. Planned derivatives include achiral X or Y groups (such as alkoxides) in compounds **B** to allow diastereoselective preparation of chiral zirconium centers. Complexes of type **C** have been prepared with peralkylated cyclopentadienyl ligands. They plan to replace one or more halogen ligands with chiral alkoxide ligands, both mono- and bi-dentate, to prepare chiral “piano-stool” structure complexes. Asymmetric transition metal catalysts are expected to lead asymmetric induction by selective binding of the substrate. Tikkanen's group plans to examine binding of Lewis bases to understand the factors that make for effective catalysts.



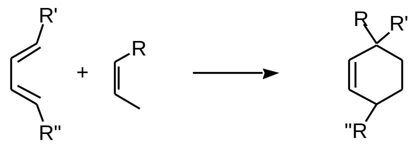
B



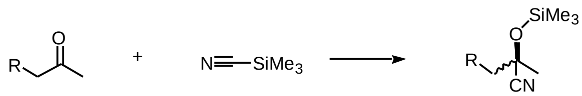
C

Reaction chemistry of the complexes

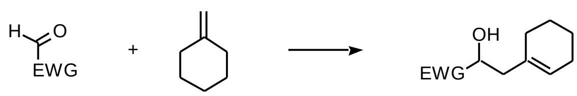
The scope of the catalytic activity and the selectivity of these Lewis acids will be tested by examining several classes of reactions, the [4+2] cycloaddition, addition of trimethylsilylcyanide to aldehydes to give cyanohydrin precursors and the oxo-ene reaction (reactions A1-A3). These reactions are known to be promoted by Lewis acids and have relatively few complicating factors such as extremely rapid and efficient Brønsted acid catalysis. In addition, these reactions have broad applications in organic synthesis and are often instrumental in synthesis of natural products and therapeutic substances.



(A1)



(A2)

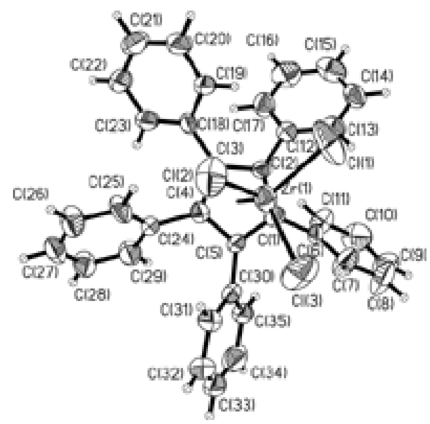


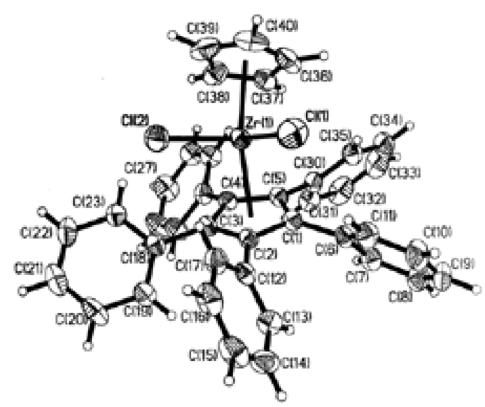
(A3)

The variety of reactions promoted by Lewis acids and the potential for asymmetric induction by the planned complexes makes the development of these new Lewis acids a challenging and rewarding field of endeavor. Students are involved in this project, from synthesis of metal complexes, choice of auxiliary groups and substrates, to analysis of project mixtures and structure determination.

CMolS and Tikkanen's work

CMolS plays a significant role in Tikkanen's work. Modeling the complexes gives us an idea of how substrates will bind to the metal. However, it is critical to know the geometry of the CpE_eZr- fragments with different coordination numbers. The piano stool, $(\eta^5\text{-}C_5Ph_5)ZrCl_3$, has significantly shorter bond distances that the sandwich complex $(\eta^5\text{-}C_5Ph_5)(\eta^5\text{-}C_5H_5)ZrCl_2$. (see next column) Structure determination allows us to obtain accurate bond distances and angles for use in modeling or in checking the validity of the results of modeling programs. Tikkanen and his students will use the structural data to refine their models and to develop a second generation of catalysts whose structures are optimized for specific substrates. Students are excited to see the effect of changing the number of ligands on parameters such as bond distance and angles and to also see some correlation with reactivity.



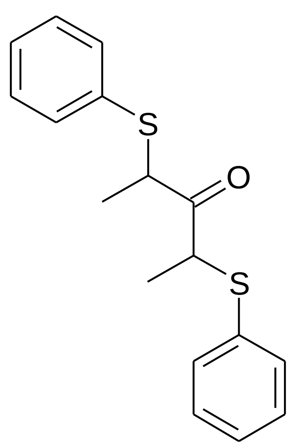


Professor Tikkanen was born in rural Rhode Island where he grew up on a farm. He received his B.S. in Chemistry from the University of Rhode Island, Kingston, and his Ph.D. from U.C. Santa Barbara. He has been on the faculty at CSULA since 1986. When not teaching or in the laboratory, Tikkanen engages in long distance cycling, photography, reading, gardening and hapkido.

Structures of Two 2,4-Arylthio-3-Pentanones: A Truly Collaborative Effort in Chemistry

CSU Fullerton

CMolS is truly a '**collaboratory**', where more than two dozen faculty and hundreds of student investigators in the CSU are brought together via Internet. They can access the necessary technology and methodology for determination and critical analysis of molecular structure, as well as actively participate in innovative courses and tutorials that require essential instrumentation and software. In the past 20 months, over 22 papers reporting work done at CMolS involving student researchers were submitted, accepted for publication or published in refereed journals.



One paper[1] represents a truly a collaborative effort in chemistry. A total of four undergraduates actively participated. The synthetic organic chemists worked under the guidance of Dr. Steven Hardinger, who is now at UCLA. Hardinger's research at CSUF investigated α,α'-bis(arylsulfonyl) ketones as new oxyallyl cation progenitors. Dimethylaryl analogs were of particular interest due to the potential for F-strain imparted by the flanking aryl methyl groups. Carbon-sulfur bond elongations were noted in the dimethylaryl series relative to the phenyl series, suggesting some F-strain to be present. The students who worked on this project were Matthew Kaller (NSF-REU, 1996), Mike McCoy (NSF-REU, 1995; BA in Chemistry, Spring 1997), and Chris Bayne (NSF-REU, 1993; BS in Chemistry, 1994). Bayne has since received a Masters in Chemistry from MIT and McCoy is in the Ph.D. program in Marine Chemistry at the Scripps Oceanographic Institute. Jacqueline Kessler (BS in Chemistry, UCSD, 1998) refined initial x-ray structures as an REU student in Prof. Katherine Kantardjieff's laboratory during the summer of 1996.

1. Guy Crundwell, Jacqueline Kessler, Matt Kaller, Mike McCoy, Christopher Bayne, Steven Hardinger and Katherine Kantardjieff. "d,1,2,4-Bis(phenylthio)-3-pentanone and d,1,2,4-bis(2',6'-dimethyl-phenylthio)-3-pentanone at 173K." *Acta Cryst*. C54 (1998).

Crystallography 101: An Introductory Course

by Dr. Bernhard Rupp
Lawrence Livermore National Laboratory

What is X-ray Crystallography ?

X-ray crystallography is an experimental technique that exploits the fact that X-rays are diffracted by crystals. It is not an imaging technique. X-rays have the proper wavelength (in the Angström range, ~10^{-8} cm) to be scattered by the electron cloud of an atom of comparable size. Based on the diffraction pattern obtained from the periodic assembly of atoms or molecules in the crystal, the electron density can be reconstructed. Additional phase information extracted either from the data or from supplementing experiments must be obtained to complete the reconstruction (the 'phase problem'). A model is then progressively built into the experimental electron density, refined against the data and the result is a quite accurate molecular structure.

Why Crystallography ?

In biosciences, the knowledge of accurate molecular structures is a prerequisite for rational drug design and for structure based functional studies in molecular medicine to aid the development of effective therapeutic agents and drugs. Crystallography can reliably provide the answer to many structure related questions, from global folds to atomic details of bonding. In contrast to NMR, which is spectroscopic and indirect method, no size limitation exists for the molecule or complex to be studied. The price for the high accuracy is that a good crystal must be found, and that only limited information about the molecule's dynamic behavior is available from a single diffraction experiment.

Crystallography 101 http://www-structure.llnl.gov/Xray/101index.html is a work in progress. After several ten thousands of visits, many users have contributed substantially to the improvement of content by either finding mistakes or suggesting new chapters or programs. Many interesting and stimulating discussions have come from students submitting answers to the quizzes. Future editions of this tutorial hopefully will contain more quizzes and answers on-line.

Any criticism as well as wishes for additions you may have is always welcome. I particularly enjoyed all the unsolicited positive response the users have provided. The kind responses are very helpful, in particular for my fund raising activities. If you have something nice to say, please let us know, in particular if you use(d) X-ray 101 in a class or course. With your help, we will be able to secure funding to expand the tutorial and make it more professional and interactive.

The next expansions will be a 2-D Patterson/Fourier map program, a full MIR solution from simple user data, and a chapter on molecular replacement. An R-free and crossvalidation page is in preparation with Brent Segelke, and the crystallization tips will be rewritten.

Again, thanks to all who have contributed in one way or the other, and I wish you fun with 101.

About the author: Dr. Bernhard Rupp heads the X-ray facility of the Biology and Biotechnology Program (BBRP) at Lawrence Livermore National Laboratory. He is also Professor of Molecular Structural Biology at the University of Vienna in Austria. Crystallography 101 is a tutorial he has created on his own without dedicated funding. Together with Dr. Rupp, CMolS is seeking funding through the National Science Foundation to expand the tutorial to make it more professional, interactive and accessible to students at all levels of the curriculum.

Upcoming Events

April 27, 1999: "Molecular Crystallography Then and Now". Seminar given by Prof. Katherine Kantardjieff at **CSU Fresno**.

April 29, 1999: "A History of Women in Science". Lecture given by Prof. Katherine Kantardjieff at the monthly dinner meeting of the San Gorgonio Section of the **American Chemical Society**.

May 22-26, 1999: **American Crystallographic Association** National Meeting, Buffalo, NY. http://nexus.hwi.buffalo.edu/ACA/ACA-Annual/Buffalo/Buffalo.html

August 4-13, 1999: **International Union of Crystallography** Meeting, Glasgow, Scotland. http://www.iucr.org/

August 22 - 26, 1999: **American Chemical Society** National Meeting, New Orleans, LA. http://www.acs.org/meetings/neworleans/welcome.htm

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